AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions, and listings, of claims in the application:

Claim 1. (Currently Amended): A method for ~~determining the presence or absence of a CYP2D6 target sequence~~ detecting specifically an allele of a pharmacologically relevant gene involved in drug metabolism in a sample ~~of DNA containing nucleic acid corresponding to CYP2D6~~, said allele comprising a target nucleotide sequence that is unique to said allele, said method comprising the steps of:

(a) contacting the sample ~~said nucleic acid~~ with a nucleic acid probe under differential hybridization ~~stringent binding conditions,~~ conditions that allow said nucleic acid probe to hybridize specifically to a nucleic acid molecule comprising said target nucleotide sequence, wherein said nucleic acid probe or said nucleic acid molecule is labeled with one or more scattered-light detectable particles of a size between 1 and 500 nm inclusive;

(b) illuminating one or more scattered-light detectable particles bound to said hybridized nucleic acid molecules using non-evanescent wave light under conditions which produce scattered light from said particle wherein light scattered from one or more said particles can be detected by a human eye with less than 500 times magnification and without electronic amplification; and

~~and detecting the presence or absence of target sequence bound with said probe, wherein said target sequence or said probe is bound with scattered-light detectable particle, and said~~

(c) detecting ~~comprises observing~~ light scattered ~~from~~ by said one or more scattered-light detectable particles under said conditions as a measure of the presence of said allele in said sample ~~particle as an indication of said presence or absence~~.

Claim 2. (Currently Amended): The method of claim 1, further comprising the step of amplifying a portion of said nucleic acid ~~corresponding to CYP2D6~~ molecule in said sample, and contacting the amplified nucleic acid molecule with said nucleic acid probe.

Claim 3. (Currently Amended): The method of claim 1, wherein said nucleic acid probe (i) is not labeled with scattered-light detectable particles and (ii) is a capture probe that is ~~a plurality of capture probes comprising nucleotide sequence complementary to nucleic acid corresponding to CYP2D6 are~~ immobilized on a solid surface, and wherein said nucleic acid molecule comprising said target nucleotide sequence is labeled with scattered-light detectable particles .

Claim 4. (Currently Amended): The method of claim 1, ~~wherein~~ further comprising ~~said determining the presence or absence of at least one target sequence in said nucleic acid corresponding to CYP2D6 comprises determining the presence or absence of a plurality of target sequences using a plurality of different probes~~ contacting the sample with a capture probe (i) that is immobilized on a solid surface and (ii) that hybridizes to said nucleic acid molecule comprising said target nucleotide sequence which is not labeled with scattered-light detectable particles, and wherein said nucleic acid probe in step (a) is labeled with scattered-light detectable particles.

Claim 5. (Currently amended): The method of claim 3 ~~claim 4~~, wherein said step (a) comprises contacting a plurality of different nucleic acid probes that differentially ~~the presence or absence of said plurality of target sequences identifies at least one CYP2D6 allele~~ hybridize to different alleles of said pharmacologically relevant gene involved in drug metabolism.

Claim 6. (Currently amended): The method of claim 5 ~~claim 4~~, wherein ~~a plurality of different nucleic acid molecules~~ said plurality of different nucleic acid probes are ~~corresponding to CYP2D6 is~~ immobilized at different spots on a solid surface.

Claims 7-8. (Canceled)

Claim 9. (Currently Amended): The method of claim 1, further comprising labeling said nucleic acid probe or said nucleic acid molecules that comprise said target nucleotide sequence by incorporating a moiety that provides an attachment site and/or a cleavage site ~~wherein said target sequence is labeled by incorporation labeling~~.

Claims 10-58. (Canceled)

Claim 59. (New): The method of claim 9, wherein said labeling step involves polymerase chain reaction, random-prime labeling, nick-translation, biased random-prime labeling, primer extension, extension displacement transcription incorporation, ligase chain reaction, ligation of multiple oligomers amplification, rolling circle amplification, strand displacement amplification, or transcription-mediated amplification.

Claim 60. (New): The method of claim 9, wherein said incorporated moiety is a modified nucleotide.

Claim 61. (New): The method of claim 9, wherein said incorporated moiety is a hapten-derivatized nucleotide or bromodeoxyuridine.

Claim 62. (New): The method of claim 61, wherein said hapten-derivatized nucleotide is derivatized with biotin, fluorescein, digoxigenin, or dinitrophenol.

Claim 63. (New): The method of claim 9, wherein said labeling step further comprises attaching said scattered-light detectable particles to said nucleic acid probe or said nucleic acid molecule comprising said target nucleotide sequence.

Claim 64. (New): The method of claim 61, wherein said labeling step further comprises attaching scattered-light detectable particles that are derivatized with anti-hapten antibodies or anti-bromodeoxyuridine antibodies to said nucleic acid probe or said nucleic acid molecule comprising said target nucleotide sequence.

Claim 65. (New): The method of claim 62, wherein said labeling step further comprises attaching scattered-light detectable particles that are derivatized with avidin or streptavidin to said nucleic acid probe or said nucleic acid molecule comprising said target nucleotide sequence.

Claim 66. (New): The method of claim 64, wherein said nucleic acid molecule that comprises said target nucleotide sequence labeled with bromodeoxyuridine are fragmented prior to hybridization with said nucleic acid probe.

Claim 67. (New): The method of claim 59, wherein said labeling step comprises using one or more primers that is a gene-specific primer or an allele-specific primer.

Claim 68. (New): The method of claim 4, wherein said step of contacting the sample with a capture probe comprises contacting the sample with a plurality of different capture probes that hybridize to different alleles of said pharmacologically relevant gene involved in drug metabolism.

Claim 69. (New): The method of claim 68, wherein said step of contacting the sample with a capture probe comprises contacting the sample with a plurality of different capture probes that are immobilized at different spots on a solid surface.

Claim 70. (New) : The method of claim 1, wherein the pharmacologically relevant gene involved in drug metabolism encodes a cytochrome P450 protein.

Claim 71. (New) : The method of claim 1, wherein the pharmacologically relevant gene involved in drug metabolism is a member of the CYP2D family.

Claim 72. (New) : The method of claim 1, wherein the pharmacologically relevant gene involved in drug metabolism is CYP2D6, CYP2C19 or CYP2C9.

Claim 73. (New) : The method of claim 72, wherein the pharmacologically relevant gene involved in drug metabolism is CYP2D6.

Claim 74. (New) : The method of claim 73, further comprising the step of demonstrating that nucleic acid sequence from CYP2D7 pseudogene, CYP2D8 pseudogene, or both is not detected.

REMARKS

I. CLAIM AMENDMENTS

Claims 1 to 58 were pending in the application. Claims 10-34 and 39-58, drawn to non-elected subject matter, are canceled without prejudice to Applicants' right to pursue the subject matter of these canceled claims in related patent applications. Claims 7-8 and 35-38 have also been canceled without prejudice. Claims 1-6, and 9 have been amended and claims 59-74 have been added to more distinctly claim Applicants' invention. No new matter has been added. Upon entry of the above-made amendment, claims 1-6, 9 and 59-74 will be pending.

Support for the claim amendments and new claims is found in the specification, as indicated in the table below.

Claims	Examples of support in the specification
Claim 1	p. 2, ll. 12-p. 3, l. 2; p. 17, ll. 28-31; p. 6, ll. 3-8; p. 7; ll. 19-21; p. 29, ll. 12-15
Claim 2	p. 5, ll. 32-p.6, ll. 2
Claim 3	p.6, ll. 12-16; p. 29, ll. 7-15.
Claim 4	p.6, ll. 12-16; p. 29, ll. 16-20.
Claim 5	p. 5, ll. 10-21; p. 7; ll. 19-21
Claim 9	p. 14, ll. 1-28; p. 29, ll. 26-28
Claim 59	p. 32, l. 6, l. 19; p. 33, l.5; p.34, l. 16; p.35, ll. 17-21
Claims 60-65	p. 29, ll.29-30; p.35, l.25-p.36, l.5; p.37, l. 37; p.38, l.8-10
Claim 66	p.38, ll. 5-12
Claim 67	p.9, ll. 5-7
Claims 68-69	p.6, ll. 12-16, ll. 25-29; p.12, ll. 1-6
Claims 70 and 71	p. 16, ll. 31 - p. 17, ll. 24.
Claims 72 and 73	p. 13, ll. 24-29
Claim 74	p. 6, l. 30-l. 7, l. 1

II. RESTRICTION REQUIREMENT

The Examiner has required a restriction under 35 U.S.C. § 121 of one of the following inventions:

I. Claims 1-9 and 35-38, drawn to methods of detecting CYP2D6 nucleic acids, classified in at least class 435, subclass 6.

II. Claims 10-34 and 39-58, drawn to a nucleic acid molecules, probes, and primers, classified in at least class 536, subclasses 23.2, 23.5, 24.31, 24.33.

The Examiner contends that the inventions are distinct, each from the other.

In order to be fully responsive, Applicants hereby provisionally elect the invention of Group I, claims 1-9 and 35-38, drawn to methods of detecting nucleic acids, classified in class 435, subclass 6, with traversal. Applicants submit that amended claims 1-6 and 9, and new claims 59-74, directed to methods of detecting an allele of a pharmocologically relevant gene involved in drug metabolism, which includes detecting an allele of CYP2D6, fall within the elected group of the invention of Group I.

Applicants retain the right to petition from the restriction requirement under 37 C.F.R. §1.144.

Applicants respectfully request that the amendments and remarks made herein be entered and made of record in the file history of the instant application.

Respectfully submitted,

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Enclosures